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Review

Nucleophilic substitution reactions of tetrafluoroethylene pentamer and tetramer and transformations of the reaction products

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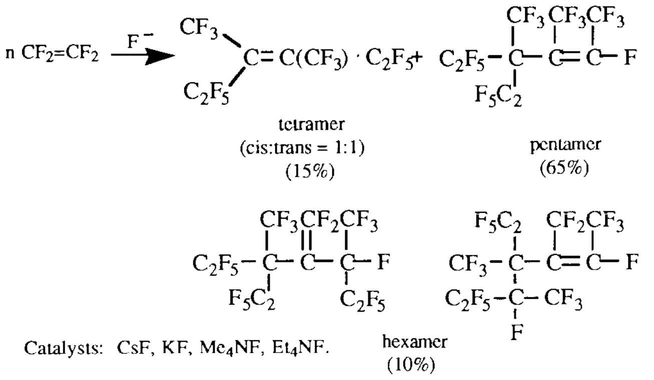
Abstract

Work carried out at the Shanghai Institute of Organic Chemistry on the reactions of tetrafluoroethylene pentamer with a variety of nucleophilic reagents such as oxygen, nitrogen and sulfur and the transformations of the reaction products is reviewed. Related reaction mechanisms, such as intramolecular nucleophilic substitution, intramolecular cycloaddition, molecular rearrangements and reaction kinetics, are also discussed.

The reactions of tetrafluoroethylene tetramer with aliphatic and aromatic amines as well as alkoxy nucleophilic reagents are also reviewed to enable a comparison with the reaction behavior of the pentamer.

Introduction

Over the past 20 or more years, one of the most interesting advances in research on perfluoro-olefins has been the oligomerization of tetrafluoroethylene (TFE). Graham of the DuPont Company in 1966 first prepared oligomers [1] ranging from the trimer to the heptamer of TFE in high yield (90%) using CsF as a catalyst. Of these oligomers, the tetramer, pentamer and hexamer were obtained as the main products.



The same result was reported simultaneously by Fielding and Jones of ICI [2] using tetramethylammonium fluoride as the catalyst, the process being expanded to an industrial scale in 1969. However, research progress on the reaction of TFE oligomer was not altogether satisfactory although to 1978 several reports were published by Chambers and co-workers [3, 4] and Coe and co-workers [5, 6]. In 1973, our group began the synthesis of oligomers of TFE using tetraethylammonium fluoride and potassium fluoride as catalysts and completed the identification of the structures of pentamer and tetramer by means of NMR, IR and MS spectra [7], followed by the syntheses of derivatives of the pentamer of TFE for use as surfactants. However, we encountered problems in the reactions of the pentamer of TFE with aliphatic nucleophiles since complex results were obtained. For this reason, it became necessary to study the reaction of oligomers of TFE with various nucleophiles under different conditions. In 1977, we reported preliminary results on the reaction of the pentamer of TFE with sodium allylic alcoholate [8]. Later, the structure of the product was revised to that of compound **2** [9]. In this review, the complex reactions of tetramer and pentamer of TFE with O-, N- and S-containing nucleophiles will be presented with possible mechanisms as a brief overview of the work carried out in the Shanghai Institute of Organic Chemistry, Academia Sinica.

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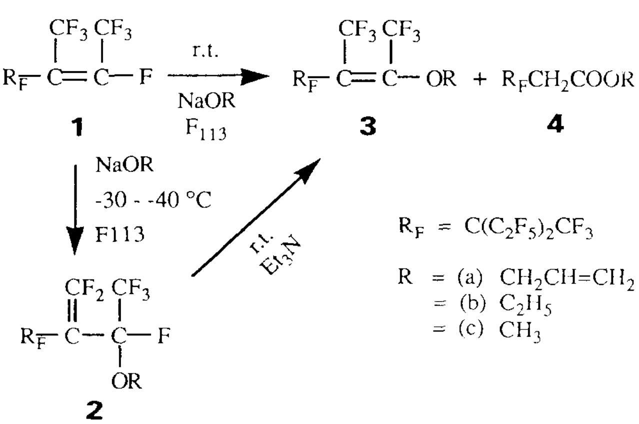
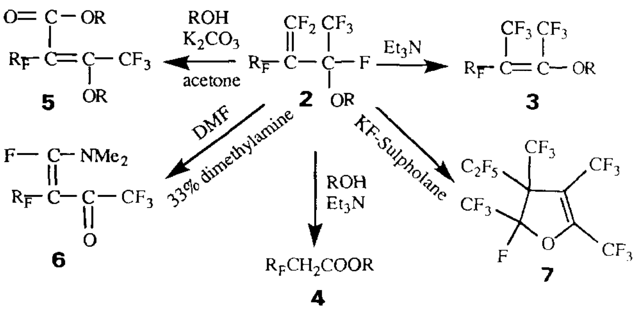
Reaction of the pentamer of TFE with alkoxide nucleophiles

The mobile double bond in the pentamer molecule means that nucleophiles can either replace a fluorine atom at a vinyl position or attack the double bond causing rearrangement towards a terminal position. When the pentamer was reacted with alkoxide nucleophiles such as allylic alcohol, methanol and ethanol at low temperature (−30 °C to −40 °C), kinetically controlled products (2) were obtained as the main products, whereas at room temperature, the main products were thermodynamically controlled (3) accompanied by small amounts of degradation products (4) [9].

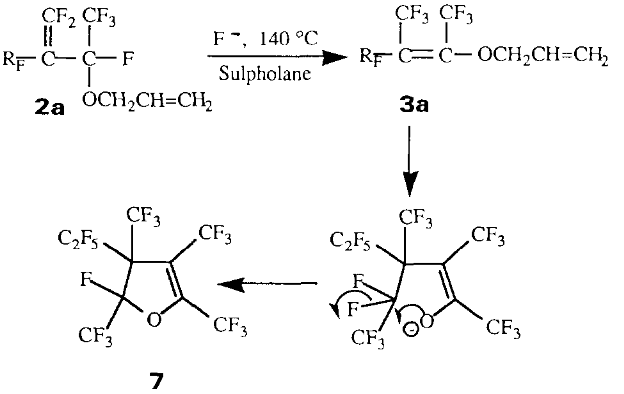


$R_F = C(C_2F_5)_2CF_3$
R = (a) $CH_2CH=CH_2$
= (b) C_2H_5
= (c) CH_3

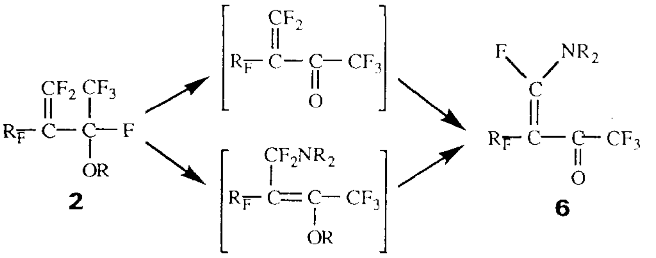
Compound 2 is capable of rearrangement to compound 3 in the presence of Et_3N at room temperature and it further reacts with other nucleophiles resulting in the unsaturated ester 5, the vinyl ketone 6, furan derivatives 7 as well as degradation products (4).



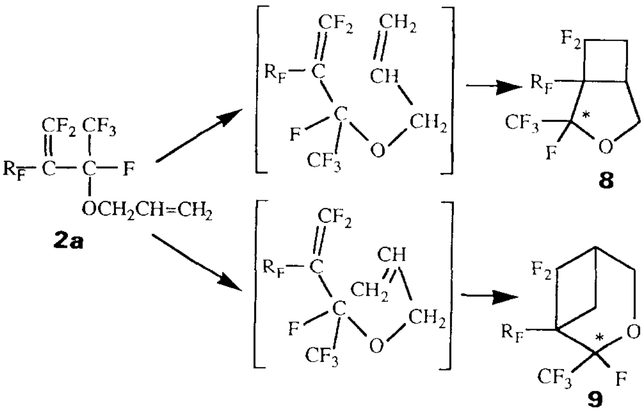
When 2a was allowed to react with KF in sulfolane at 140 °C, the furan derivative 7 was formed. This probably occurred via the intermediate 3a. Attack via intramolecular nucleophilic substitution of an oxyanion arising from the cleavage of the alkyl–oxygen bond [10] on difluoromethylene led to ring-closure to give the furan 7 [3]. Similar results may be obtained when R in 3 is Me [11]. NMR spectroscopic analysis of the reaction showed that 2a was nearly completely converted to 3a after 2 h, and 7 h later 100% conversion to 7 had occurred. This result was supported by the fact that compound 3a was directly converted into 7 under the same conditions; the structure of compound 7 being consistent with the report [3] by Chambers *et al.* that the pentamer of TFE reacts with H_2O/Et_3N to give furan 7.



When compound 2 was allowed to react with dimethylamine, the enamine ketone 6 was obtained via the following two possible routes:



When compound 2a was heated at 140 °C in the absence of solvent and catalyst it gave the intramolecular [2+2] cycloaddition products 8 [3.2.0] and 9 [3.1.1] as well as polymer 10 [12].

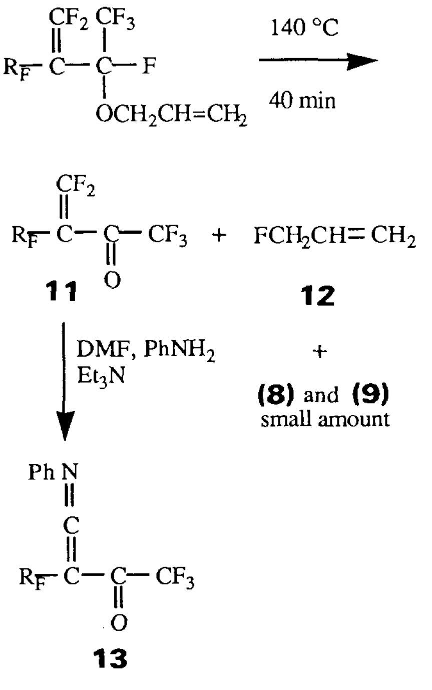


Polymer **10**

TABLE 1. The effect of reaction temperature on the product composition

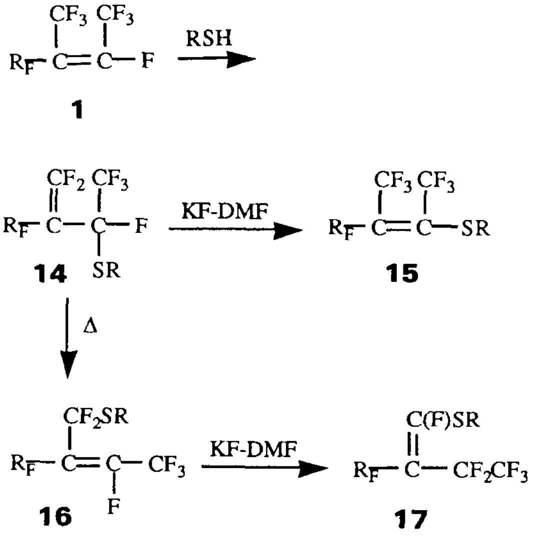
Products (%)	−60 to −50 °C	−35 to −30 °C	−20 to −10 °C	13 °C	34 °C
14	100	95.2	71.9	37.5	13.3
15	0	4.8	28.1	62.5	86.7

When R in compound **2** is a methyl group, no intermolecular cycloaddition products were observed even at 170 °C. When the allylic ether $(CH_2=CHCH_2)_2O$ was heated under the same conditions, no cycloaddition product was found. This shows that [2+2]-cycloaddition reaction only occurs between the fluorine-containing double bond and the allylic double bond, i.e. intramolecular cycloaddition led to products **8** and **9** while intermolecular cycloaddition led to polymer **10**. Hence, a concerted or biradical process may be involved in the reaction. When compound **2a** was heated at 140 °C in an NMR tube, **11** and **12** were obtained as the main products, along with a small amount of the above addition products (**8** and **9**). The vinyl ketone **11** could be converted readily into the corresponding carbonyl ketenimine **13** [12].



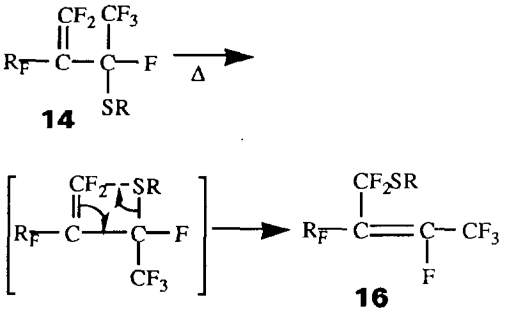
Reaction of the pentamer of TFE with S-containing nucleophiles

When the pentamer of TFE was allowed to react with mercaptans such as allylic thiol, benzyl thiol and phenyl thiol in the presence of Et_3N, four types of isomer were obtained [13, 14]. Below −30 °C, the kinetically controlled products [14] were formed, whereas at room temperatures the thermodynamically controlled products **15** were obtained as the main products. The effects of reaction temperature on the product composition are listed in Table 1. Compound **14** can be converted into **15** employing the KF/DMF system.



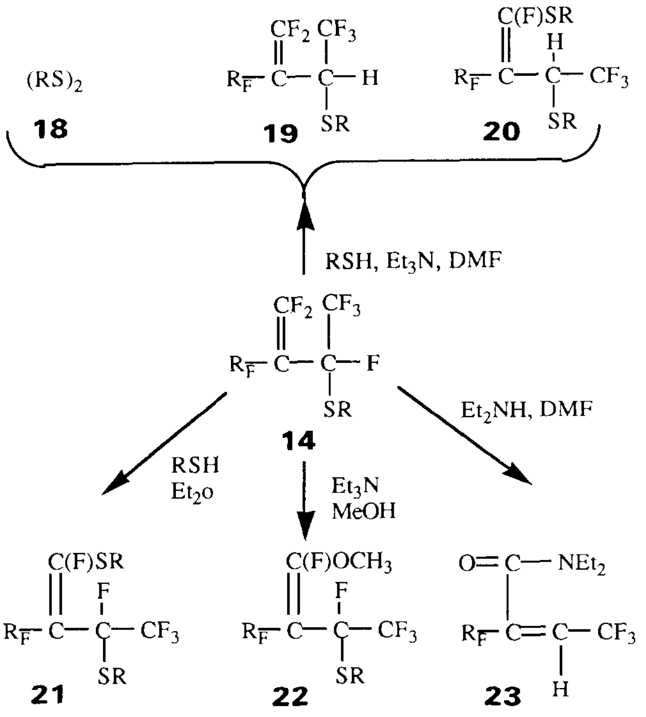
R = (a) $PhCH_2$, (b) $CH_2CH=CH_2$, (c) C_6H_5

It is noteworthy that compound **14** rearranges spontaneously to isomer **16** when allowed to stand for several weeks at room temperature; this change is accelerated on increasing the temperature. The rearrangement of **14** to **16** may involve a 1,3-shift process via the four-membered ring transition state as shown:



Kinetic studies [15] indicated that the reaction obeyed first-order kinetics. The reaction rate was not retardated by inhibitors such as *p*-dihydroxybenzene and dinitrobenzene, and was not dependent upon the polarity of the solvents. Hence, the reaction most likely proceeds through an intramolecular nucleophilic rearrangement. The negative value of the entropy change of the reaction, $\Delta S^{\ddagger}$, indicates that a more ordered transition state might be involved in the process. Compound **16** is readily converted to **17** in the presence of KF/DMF.

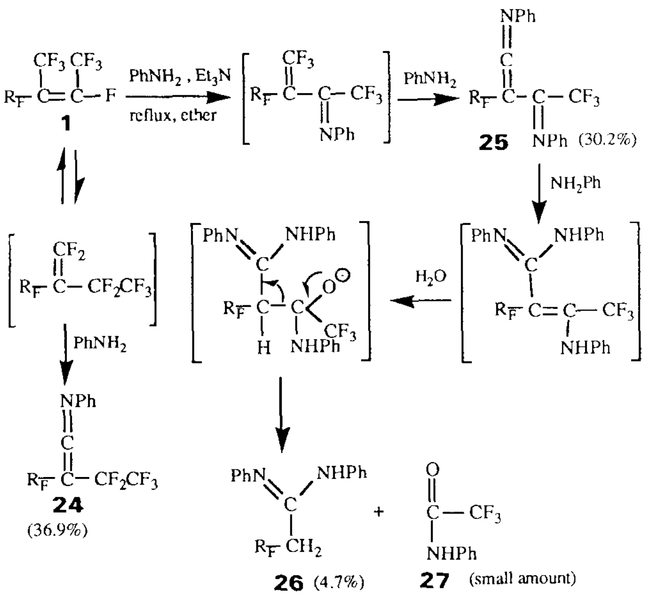
The more reactive compound **14** is much more susceptible to nucleophiles such as dimethylamine, methanol and mercaptans, leading to compounds **18–23** respectively [13, 14].



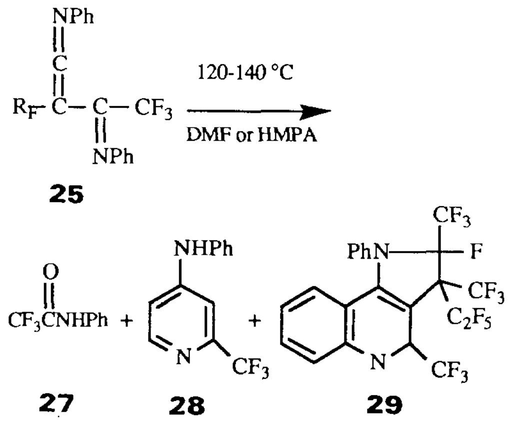
It is interesting to note that the product **19** contains a proton in the molecule. For such an unusual product to be formed, a 1,4-elimination mechanism [16] or an electron-transfer process may be involved in the reaction [17].

Reaction of the pentamer of TFE with amines

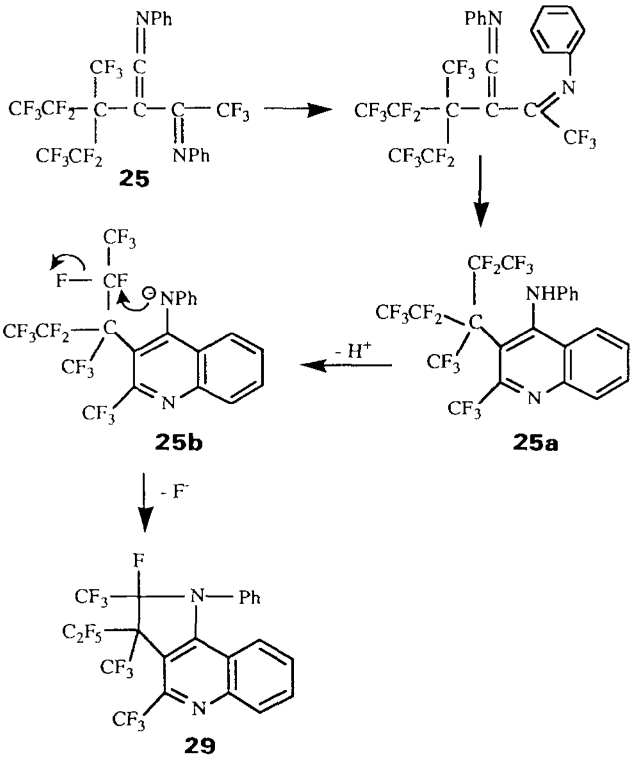
The pentamer of TFE is normally unreactive towards aromatic amines. However, on reflux in ether in the presence of triethylamine, the reaction gave the products **24–27**, respectively [18, 19].



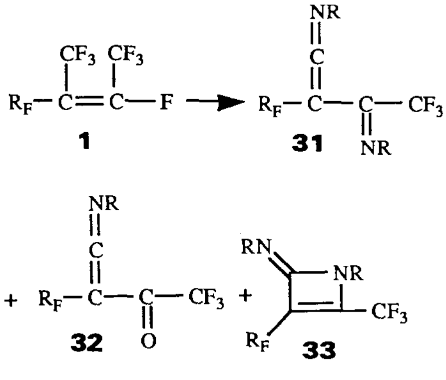
When compound **25** was heated in a polar aprotic solution for 15 h at 120–140 °C, in addition to **27** and **28**, small amounts (2.6%) of the fused product were obtained. In HMPA as the solvent, an approximately 65% yield of **29** was obtained.



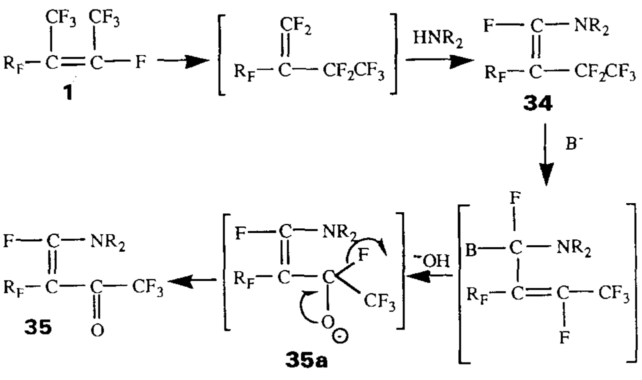
It was considered that compound **25** first undergoes ring-closure to the intermediate **25a** [20], which then loses a proton to form the anion **25b**. Subsequently, intramolecular nucleophilic substitution on difluoromethylene leads to **29**. The process is very similar to that occurring with oxyanions as previously described. To our knowledge, there appears to be no precedent for this reaction in organofluorine chemistry [21].



When the pentamer of TFE was allowed to react with aliphatic primary amines [22] such as n-butylamine or methylamine, imino ketenimine **31**, carbonyl ketenimine **32** and azetidine **33** were obtained.



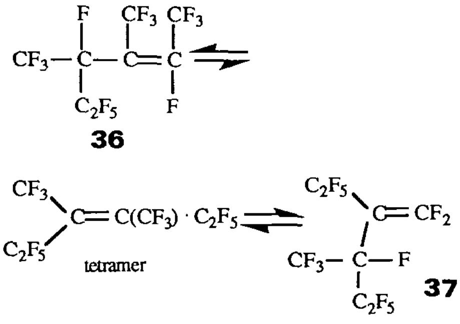
Clearly, compound **33** is an intramolecular addition product of **31**; however, it was not observed in the reaction of aromatic amines. When **1** reacts with aliphatic secondary amines [22] such as dimethylamine, diethylamine, morpholine and piperidine, the unstable enamines **34** are formed, which undergo hydrolysis to give the vinyl ketones **35**. The same products may also be obtained by way of the intermediate **11** which further reacts with HNR_2 to give **35**.

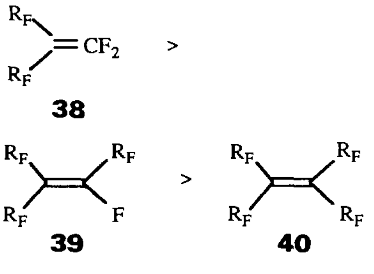


$R_2 = Me_2, Et_2, CH_2CH_2OCH_2CH_2, (CH_2)_5$

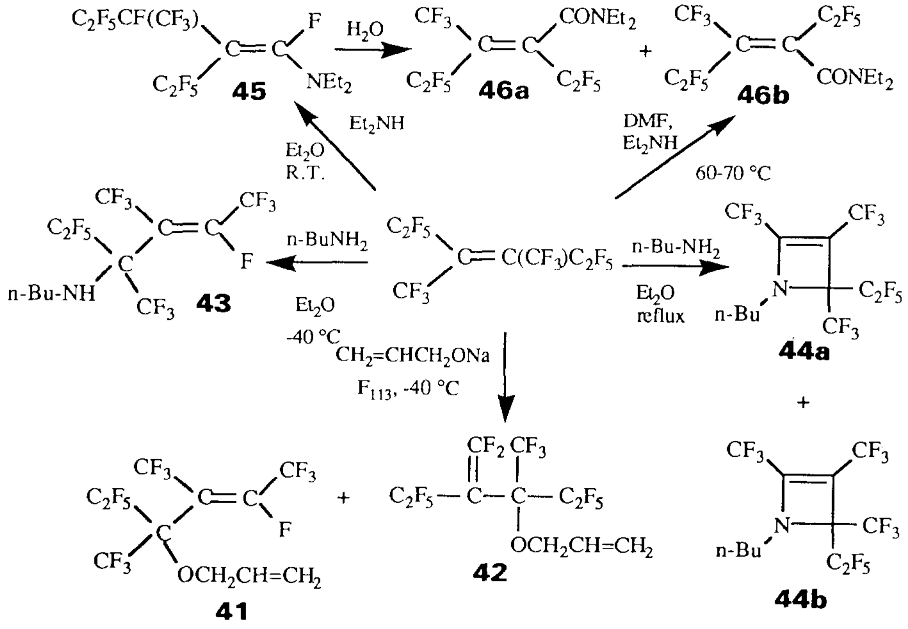
The reactions of TFE tetramer with nucleophiles

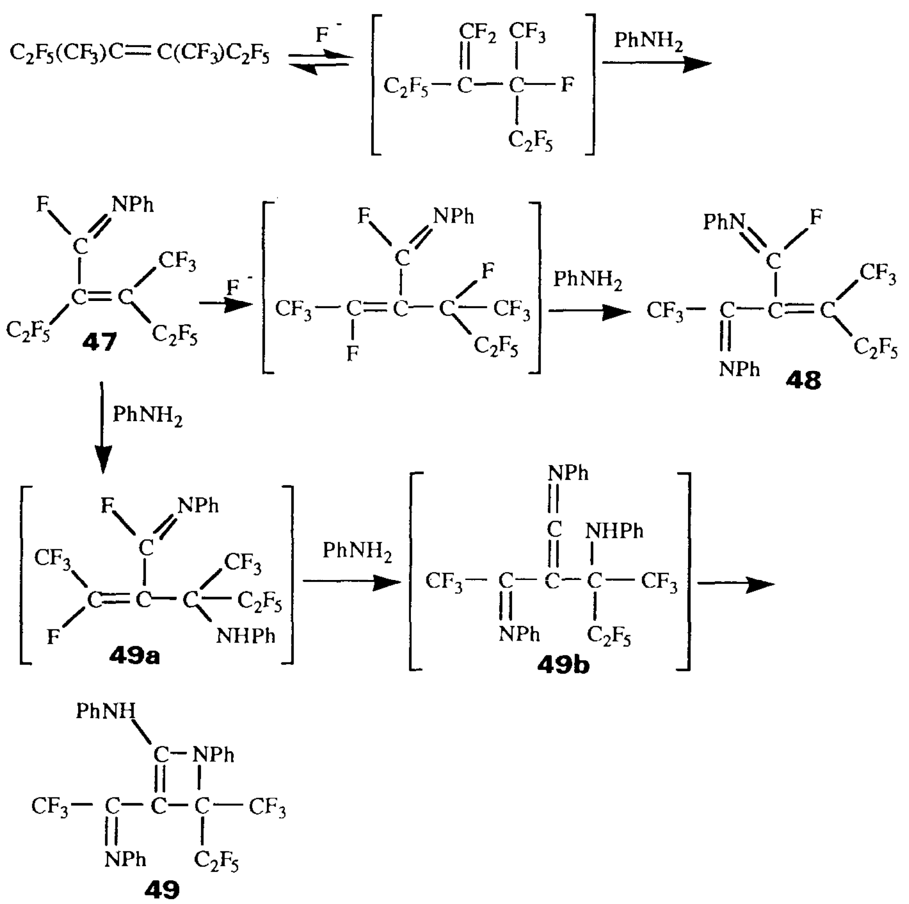
Because of its very mobile double bond, the tetramer of TFE reacts with nucleophiles to give more complex products than the pentamer. Chambers and Lindley reported [23] that in the presence of the fluoride ion, the tetramer is in equilibrium with its two isomers (**36** and **37**). They also pointed out that the terminal fluoroolefin **38** is more reactive than those containing vinyl fluorines (**39**). The activity of perfluorotetraalkyl-substituted olefin **40** is less than that of **39**.





When the tetramer reacted with aliphatic alkoxide nucleophiles, the isomers **41** and **42** were obtained [24]. With aliphatic primary amines at −40 °C in Et_2O, it gave **43** and under reflux it formed the azetidines **44a** and **44b** [24]. When aliphatic secondary amines were

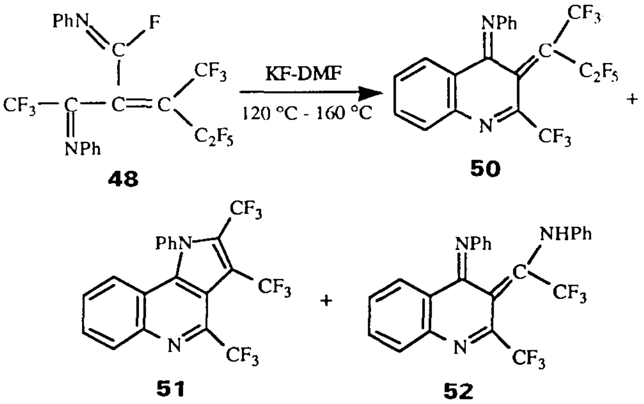




reacted with the tetramer in anhydrous diethyl ether, an unstable enamine **45** was obtained [4, 24], which very readily hydrolyzed to the amides **46a** and **46b** [24].

No reaction occurred below 0 °C when the tetramer was reacted with aromatic amines. Only under reflux was it possible to obtain **47** and **48** together with small amounts of the cyclic products **49**. The composition of products varied with the mole ratio of the reactants. Compound **47** reacted with another mole of aniline in a 1:1 ratio to give **48** (40%) and **49** (26%) [18, 19]. However, **48** was not converted to **49** under the same conditions. This indicates that a greater degree of conjugation and steric hindrance exists in **48** than in **49a**. In contrast, compound **47** was more reactive than **48**. It is possible that **49** stems from the intermediates **49a** and **49b**.

When **48** was heated in saturated KF/DMF solution [18, 19] for 12 h at 120–160 °C, small amounts of the closed ring products **50**–**52** were obtained and in HMPA higher yields of **51** were formed. These results were supported by X-ray diffraction data [25].



48 **50** **51** **52**

We have attempted to study the reaction of TFE tetramer with sulfur-containing nucleophiles. However, complex mixtures were obtained and we have not separated pure compounds to date.

The reactions of TFE hexamer with nucleophiles were reported by Coe *et al.* [26, 27] who also proposed a single electron transfer mechanism for the ring-closure of the oxyanions of TFE pentamer [28].

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